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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,980	09/24/2004	Ryuji Kaji	TOYA140.001APC	1114

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EXAMINER	
KOSSON, ROSANNE	

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
11/07/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/508,980	KAJI ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-13,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on September 29, 2008 has been received and entered. Claim 8 has been amended. Claims 1-7 and 14 were canceled in previous amendments. No claims have been added. Accordingly, claims 8-13, 15 and 16 are examined on the merits herewith.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 8-13, 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Bigalke et al. (WO 00/74703 A2, published on Dec. 14, 2000), the English language equivalent of which is CA 2376193 C (the Canadian national phase application was originally published in German). Because Applicants are Japanese and not German, the English language publication will be referred to for convenience. Applicants are also referred to pp. 1-3; p. 4, 4th paragraph; and p. 5, 3^{d} and 4th paragraphs of the PCT publication.

Bigalke et al. disclose a method of treating various nervous system disorders, including a variety of dystonias and muscle spasticities (see paragraph bridging pp. 1-2; p. 4, first full paragraph; and p. 8, first paragraph). Bigalke et al. disclose a pharmaceutical preparation of *Clostridium botulinum* toxin subunits that is free of the complexing proteins (the non-toxic subunits) for treating these disorders. The toxic subunits may be of the same type, one of types A-G, or of mixed types, such as A and B (see p. 1, 1st paragraph; and p. 7). Bigalke et al. disclose that the purpose of removing the non-toxic subunits is to make the toxin less immunogenic, because subjects develop antibodies to the highly immunogenic hemagglutinin subunits, which cause immune responses in the subjects and render the toxin ineffective as a drug (see pp. 2-4). A second purpose is to create a smaller protein complex that diffuses more rapidly to the target cells (see top of p. 5). Bigalke et al. note that, in the native form, the non-toxic subunits protect the toxic subunits from degradation in the gastrointestinal tract but that this protection is not needed if the toxin-containing preparation is injected parenterally or into muscles at the site(s) where it is needed (see bottom of p. 2 and top of p. 3).

Bigalke et al. disclose that the toxin is prepared in a stabilizing solution of sucrose and human serum albumin and that the preparation is lyophilized for storage (see p. 10, Example 2).

Regarding claim 9, each of the diseases treated in the method of Bigalke et al. requires a fast-acting remedy, as these diseases cause considerable discomfort and pain.

In view of the foregoing, a holding of anticipation is required.

Claim Rejections - 35 USC § 103

In view of Applicants' amendments to the claims, these rejections are withdrawn.

Nevertheless, some of Applicants' comments require a reply for correction or clarification. In their remarks, Applicants assert that Johnson et al. are completely silent on the use of their pharmaceutical composition and that they do not teach the use of any botulinum neurotoxin for treating muscle hyperactivity. Applicants assert that neither Johnson et al. nor Borodic disclose that removing the non-toxic subunits from the complex reduces antigenicity. Applicants assert that, although Aoki et al. disclose adding human serum albumin to their botulinum toxin preparation, they do not disclose that it has a stabilizing effect.

In reply, the first two points have been addressed in all of the previous Office actions. To reiterate, Johnson et al. disclose that purified preparations of *C. botulinum* toxins are used to treat involuntary muscle disorders and that some of the non-toxic proteins in the complex have hemagglutinating ability and are antigenic (see col. 5, lines 47-67). Johnson et al. disclose that the advantage of their mixed preparation, containing light and heavy toxin chains of different types, compared to commercial preparations, is that it retains the activity of a preparation of light and heavy chains from the same type, and is even longer acting, but it is less antigenic (see col. 6, lines 12-46). Regarding Aoki et al., bovine serum albumin (BSA) and human serum albumin (HSA) are considered in the art to be conventional stabilizing agents for proteins. Obviously, for in vivo use, HSA is less antigenic than BSA. The preparation steps and reagents disclosed in col. 4 are all presented as being conventional in the art, not as being novel to Aoki et al.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is (571)272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rosanne Kosson
Examiner, Art Unit 1652

rk/2008-10-02

/JON P WEBER/

Supervisory Patent Examiner, Art Unit 1657